ABSTRACT OF THE DISCLOSURE

A self-renewing restricted stem cell population has been identified in developing (embryonic day 13.5) spinal cords that can differentiate into multiple neuronal phenotypes, but cannot differentiate into glial phenotypes. This neuronal-restricted precursor (NRP) expresses highly polysialated or embryonic neural cell adhesion molecule (E-NCAM) and is morphologically distinct from neuroepithelial stem cells (NEP cells) and spinal glial progenitors derived from embryonic day 10.5 spinal cord. NRP cells self renew over multiple passages in the presence of fibroblast growth factor (FGF) and neurotrophin 3 (NT-3) and express a characteristic subset of neuronal epitopes. When cultured in the presence of RA and the absence of FGF, NRP cells differentiate into GABAergic, glutaminergic, and cholinergic immunoreactive neurons. NRP cells can also be generated from multipotent NEP cells cultured from embryonic day 10.5 neural tubes. Clonal analysis shows that E-NCAM immunoreactive NRP cells arise from an NEP progenitor cell that generates other restricted CNS precursors. The NEP-derived E-NCAM immunoreactive cells undergo self renewal in defined medium and differentiate into multiple neuronal phenotypes in mass and clonal culture. Thus, a direct lineal relationship exists between multipotential NEP cells and more restricted neuronal precursor cells present *in vivo* at embryonic day 13.5 in the spinal cord. Methods for treating neurological diseases are also disclosed.